

**Amendments to the Specification**

Please amend the Specification (as-published) as follows:

**(1) Please amend paragraph [0013] of the Specification as-published as follows:**

[0013] 12) a coated preparation obtained according to the production method of the aforementioned 1), which shows elution of not less than 50% of pioglitazone hydrochloride in 15 minutes in a dissolution test by a ~~puddle~~ paddle method using a hydrochloric acid-potassium chloride buffer (pH 2.0) as a test solution at 37° C, 50 rpm; and the like.

**(2) Please amend paragraph [0080] of the Specification as-published as follows:**

[0080] The present invention moreover relates to "a coated preparation obtained according to the production method of the present invention, which shows elution of not less than 50% of pioglitazone hydrochloride in 15 minutes in a dissolution test by a ~~puddle~~ paddle method using a hydrochloric acid-potassium chloride buffer (pH 2.0) as a test solution at 37° C, 50 rpm". As used herein, the dissolution test is performed according to the method described in The Japanese Pharmacopoeia 14th Edition. The "hydrochloric acid-potassium chloride buffer (pH 2.0)" used as a test solution can be prepared according to a known method. The amount of the hydrochloric acid-potassium chloride buffer used as a test solution is generally 900 mL.

**(3) Please amend paragraph [0081] of the Specification as-published as follows:**

[0081] The "coated preparation obtained according to the production method of the present invention, which shows elution of not less than 50% of pioglitazone hydrochloride in 15 minutes in a dissolution test by a ~~puddle~~ paddle method using a hydrochloric acid-potassium chloride buffer (pH 2.0) as a test solution at 37° C, 50 rpm" can be administered orally and safely to mammals (e.g., mouse, rat, rabbit, cat, dog, bovine, horse, monkey, human and the like), as the aforementioned coated preparation of the present invention, wherein the target disease, dose and the like are the same as those in the aforementioned coated preparation of the present invention.

**(4) Please amend paragraph [0093] of the Specification as-published as follows:**

[0093] The coated preparations obtained in the aforementioned Example 2 and Example 3 were evaluated for the dissolution property of pioglitazone hydrochloride by a ~~puddle~~ paddle method (50 rpm) using a 0.3 M hydrochloric acid-potassium chloride buffer (900 mL, 37° C, pH 2.0). The results are shown in Table 2.

## **REMARKS**

The Applicants thank the Office for withdrawing the previous objection and rejections under 35 U.S.C. §§ 112, 102(b), and respectfully request reconsideration of the present application in view of the foregoing amendments and the reasons that follow.

### **I. Status of Specification and Claims**

Minor typographical errors in the Specification are corrected, as shown on page 4 of this submission. Independent claims 1 and 10 are amended to clarify that the organic solvent contains polyvinylpyrrolidone as a coating base soluble in organic solvents; support for the amendments can be found in, for example, lines 2-22 on page 5 of the Specification as-filed and original claim 3. Support for the new claims 13 and 14 can be found in, for example, line 29 on page 19 to line 23 on page 20 of the Specification as filed. No new matter is introduced, and claims 1, 4-8, 10, and 13-14 are currently pending to be examined on their merits.

### **II. Claim Rejection - 35 U.S.C. § 103**

The Office alleges that claims 1 and 3-10 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Timmins (US 6,031,004) in view of Cutie (WO 91/82875). The Applicants respectfully disagree and traverse the rejection. Additionally, in view of the previous reply filed August 20, 2008, the Applicants assume that the Office on page 4 of the Office Action refers to claims 1, 4-8, and 10 and thus provide the following analysis accordingly.

#### **(i) Timmins and Cutie Do Not Teach/Suggest Every Element in the Present Claims**

While not acquiescing to the grounds of rejections, independent claims 1 and 10 are amended to clarify that it is the organic solvent in the dispersion used to coat a core that contains polyvinylpyrrolidone. The Office acknowledges that Timmins does not disclose polyvinylpyrrolidone as a base in an organic solvent. Page 6, Office Action. With the present amendment, the Applicants have further distinguished Timmins' teaching from the present claims.

The presently claimed methods are related to coating a core containing an active ingredient with a dispersion of pioglitazone hydrochloride in an organic solvent, which organic solvent contains polyvinylpyrrolidone as a coating base soluble in organic solvents.

Nowhere does Timmins teach or suggest that pioglitazone is **applied to the surface of a core of a metformin salt** – instead, Timmins discloses only a concurrent use of pioglitazone with a metformin salt. For instance, the polyvinylpyrrolidone pointed out as a binder by the Office is used in a tablet (col. 5, lines 16-19, Examples 3 and 5, Timmins), and the use thereof for a coating layer covering the tablet core is not described at all in Timmins.

Cutie does not cure the deficiencies mentioned above. Cutie teaches a core with a first layer comprising pioglitazone hydrochloride (Cutie, page 2, lines 20-30). Nowhere does it teach that the pioglitazone is in a dispersed form in an organic solvent containing polyvinylpyrrolidone, as presently claimed. Thus, according to the obviousness determination standard as delineated by the U.S. Supreme Court in *KSR* and explained in the previous August 20, 2008 reply, one of ordinary skill in the art would not have a reason to combine the teachings of Timmins and Cutie. Further, even assuming, *arguendo*, that the teachings of Timmins and Cutie were combined, the presently claimed methods and coated preparation produced thereby would not result.

Thus, Timmins and Cutie, alone or in combination, cannot render the independent claims 1 and 10, and their dependent claims, obvious.

(ii) *Timmins and Cutie Do Not Provide the Unexpected Results as Presently Claimed*

The presently claimed methods are also non-obvious over Timmins and/or Cutie in view of the unexpected desirable results with respect to the superior dissolution property provided by the coated preparation produced by the presently claimed methods. See e.g., lines 9-14 on page 21 of the present Specification. Neither Timmins nor Cutie teaches or suggests a method that can produce a preparation with such a property, as presently claimed. In fact, even if the

teachings of Timmins and Cutie were combined, such an unexpected desirable properties would still not result.

To demonstrate such an unexpected desirable result, the Applicants respectfully submit herewith a Rule 132 declaration by Mr. Masahiko Koike, a co-inventor of the present application, to show the unexpected beneficial effect of using an organic solvent to coat a core, as presently claimed. As clearly shown in the Koike Declaration (see e.g., Table A), a coated preparation produced with an organic solvent as presently claimed (“Example 1”) shows a dissolution rate of pioglitazone hydrochloride unexpectedly higher (and thus superior) than one produced with distilled water (“Comparative Example 1”).

In addition to the differences pointed out in the previous section of this submission, neither Timmins nor Cutie teaches or suggests a method of producing a preparation with the unexpected desirable dissolution property of pioglitazone hydrochloride as provided by the presently claimed preparation. In fact, even if the teachings of Timmins and Cutie were combined, a coated preparation with such an unexpected superior dissolution property, in particular with respect to the dissolution rates as recited in new claims 13 and 14, would not result. Thus, the Applicants further respectfully submit that claims 13 and 14 are separately patentable.

Therefore, at this in view of the foregoing, the Applicants respectfully request that the rejection be withdrawn.

**CONCLUSION**

The Applicants believe that the present application is now in condition for allowance and thus respectfully request favorable reconsideration of the application.


The Office is invited to contact the undersigned by telephone if a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application, or credit any overpayment, to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicants hereby petition for such extension under 37 C.F.R. § 1.136 and authorize payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 672-5569  
Facsimile: (202) 672-5399

By 

Stephen B. Maebius  
Attorney for the Applicants  
Registration No. 35,264